

[0131] 86. The cell culture system of any one of claims 54-85, wherein the cell culture medium is a protein-free cell culture medium.

[0132] 87. The cell culture system of any one of claims 54-86, wherein the cell culture medium is selected from the group consisting of MEM, DMEM, RPMI, Ham's F-12 medium, Leibovitz's L-15 medium, and mixtures thereof, said medium being supplemented with one or more tonicifying agents.

[0133] 88. The cell culture system of any one of claims 54-86, wherein the cell culture medium consists essentially of DMEM supplemented with one or more tonicifying agents

[0134] 89. The cell culture system of any one of claims 54-88, wherein the host cell is a mammalian cell.

[0135] 90. The cell culture system of claim 89, wherein the host cell is selected from the group consisting of HeLa, HEK293, COS, A549, BHK, and Vero cells.

[0136] 91. The cell culture system of claim 90, wherein the host cell is a HeLa cell.

[0137] 92. The cell culture system of any one of claims 54-88, wherein the host cell is an insect cell.

[0138] 93. The cell culture system of claim 92, wherein the host cell is selected from the group consisting of Sf9, Sf-21, Tn-368, and BTI-Tn-5B1-4 (High-Five) cells.

[0139] 94. The cell culture system of any one of claims 54-93, wherein the helper virus is selected from the group consisting of adenovirus, herpes virus, baculovirus, and recombinant forms of any of the foregoing viruses.

[0140] 95. The cell culture system of any one of claims 54-91, wherein the helper virus is an adenovirus (AV).

[0141] 96. The cell culture system of claim 95 wherein the helper virus is Ad5.

[0142] 97. The cell culture system of any one of claims 54-96, wherein the host cell comprises a heterologous nucleotide sequence flanked by AAV inverted terminal repeats.

[0143] 98. The cell culture system of any one of claims 54-96, wherein the host cell comprises rep and cap genes.

[0144] 99. The cell culture system of any one of claims 54-96, wherein the host cell comprises helper virus genes.

[0145] 100. The cell culture system of any one of claims 54-96, wherein the host cell comprises a heterologous nucleotide sequence flanked by AAV inverted terminal repeats, rep and cap genes, and helper virus genes.

INCORPORATION BY REFERENCE

[0146] The entire disclosure of each of the patent and scientific documents referred to herein is incorporated by reference for all purposes.

EQUIVALENTS

[0147] The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting on the invention described herein. Scope of the invention is thus indicated by the appended claims rather than by the foregoing description, and all changes that come within the meaning and range of equivalency of the claims are intended to be embraced therein.

What is claimed is:

1. A method for producing a recombinant adeno-associated virus vector (rAAV) using a helper virus, the method comprising incubating a host cell capable of producing rAAV in the presence of helper virus for an incubation period in a cell culture medium containing helper virus and one or more tonicifying agents and having an osmolality of 360 mOsm/kg or higher at the start of the incubation period.

2. The method of claim 1, wherein the host cell is also capable of producing helper virus.

3. The method of any preceding claim, wherein the host cell comprises a genome, said genome comprising one or more AAV genes stably integrated therein.

4. The method of any preceding claim, wherein the cell culture medium has an osmolality of 375 mOsm/kg or higher at the start of the incubation period.

5. The method of any preceding claim, wherein the cell culture medium has an osmolality of 400 mOsm/kg or higher at the start of the incubation period.

6. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce a 20% reduction in total helper virus production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

7. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce a 30% reduction in total helper virus production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

8. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce a 40% reduction in total helper virus production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

9. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce a 50% reduction in total helper virus production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

10. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce at least a 50% increase in total rAAV production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

11. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce at least a 100% increase in total rAAV production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

12. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce at least a 150% increase in total rAAV production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

13. The method of any preceding claim, wherein the cell culture medium has an osmolality at the start of the incubation period sufficient to produce at least a 200% increase in total rAAV production compared to a host cell incubated in a medium with an osmolality of 266 mOsm/kg.

14. The method of any preceding claim, wherein at least one tonicifying agent is an ionic tonicifying agent.

15. The method of any preceding claim, wherein at least one tonicifying agent is selected from the group comprising: